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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,464	02/11/2002	James Tiedje	MSU-06787	4392

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EXAMINER	
BAUSCH, SARAE L	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
09/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/073,464	TIEDJE ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-14,16 and 22-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-14,16 and 22-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1-6, 8-14, 22-27 are pending in the instant application. Claim 7 and 15-21 have been canceled. This action is written in response to applicant's correspondence submitted 06/09/2008. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented, necessitated by the amendment to the claims or are reiterated from the previous office action. Any rejections not reiterated in this action have been withdrawn as necessitated by applicant's amendments to the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is Final.

Withdrawn Rejections

2. The rejections of claims 1-6, 8-14, and 22-27, under 35 U.S.C. 103, made in section 11, of the previous office action mailed 02/08/2008, is withdrawn in view of the amendment to the claims.

3. The rejections of claims 1-5 and 8-13 under 35 U.S.C. 103, made in section 13, of the previous office action mailed 02/08/2008, is withdrawn in view of the amendment to the claims.

New Grounds of Rejection, Necessitated by Amendment to the claims

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-6, 8-14, and 22-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is newly presented, necessitated by the amendment to the claims.

The amendment to claims 1 and 9, with the recitation "identifying without the need for sequencing said amplified genomic sequences" is not supported in the specification and raises the issue of new matter. The specification teaches that genomic DNA was fragmented to ensure randomness and fragments were size fractionated, eluted, and purified. The specification teaches that the genomic DNA fragments were inserted into pPCR-Script Amp vector and PCR amplified using standard PCR conditions, followed by purification and quantification (see pg 32 lines 5-18). The specification however is silent with respect to sequencing the amplified genomic sequences and thus identifying without the need for sequencing. The amendment to recite "identifying without the need for sequencing said amplified genomic sequences" encompasses any non-sequencing based identification method and the specification does not provide support for the broad genus of identification methods encompassed by the claims. The specification does provide support for identifying species of test bacteria by array hybridization (see pg. 35, lines 3-10). As the specification does not provide support for identifying bacteria with *or* without sequencing the amplified genomic sequences, it is not clear that the inventor's contemplated identifying bacteria with *or* without sequencing. As the amended claims recite a

limitation that the specification does not contemplate, as the specification only contemplated identification by array hybridization and does not contemplate any type of identification method that is not based on sequencing the amendment to the claims constitutes new matter.

Maintained Rejection

6. Claims 22-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection was previously presented in section 8 and is reiterated below.

Claims 22-25 with the recitation of "at least 60 arrayed elements" and "at least 90 arrayed elements" and the subgenus of "at least 60" and "at least 90" is not supported in the specification and raises the issue of new matter. The specification teaches 60 to 96 genome fragments were spotted on microarrays (see page 7, lines 5-6). The specification teaches that arrays containing up to approximately 100,000 DNA spots are used (see page 7, lines 20-22). However the specification does not teach "at least" 60 or "at least" 90 arrayed elements. The specification provides no indication of the criticality of the amended range.

As discussed in MPEP 2163.05, section III, with respect to changing numerical range limitations, the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure. Purdue Pharma L.P. v. Faulding Inc., 230 F.3d 1320, 1328, 56 USPQ2d1481, 1487 (Fed. Cir. 2000) ("[T]he specification does not clearly disclose to the skilled artisan that the inventors... considered the...

ratio to be part of their invention.... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion").

Response to Arguments

7. The resposne traverses the rejection on pages 8-9 of the remarks mailed 06/09/2008. The resposne asserts that the specification teaches the use of arrays containing 60, 90, 92, 96, 380, 338, 100,000, less than 100,000 more than 100,000 and 500,000 reference genomic sequences and thus confirms the understanding that the inventors contemplated "at least 60" and "at least 90" arrayed reference genomic sequences. The response points to the specificaiton for support of 380 and 500,000 genome sequences and smaller and large numbers than 100,000 genomic sequences. The examiner agrees that the specificaiton does provide support for 338 spotted fragments (see pg. 8 lines 11-12), as well as 92, 90, 96, and 60 fragments (see pg. 32 lines 20-21), in addition to 500,000 probes (see pg. 11, lines 14-15) however the specification does not provide support for 'more than 100,000' and 'less than 100,000' as asserted by applicants in the remarks mailed 06/09/2008. It is noted that the specification does not contemplate "more than 100,000" as this encompasses more than 500,000 and the specification does not contemplate more than 500,000 probes on an array, although the claims recite "at least 60" and "at least 96" which have no upper limit and thus encompass more than 500,000 probes which is not contemplated in the specification.

The response asserts on page 9 that MPEP 2163.05 section III, *In re Wertheim*, found that there was adequate written description support for the claimed range between 35% and 60% because the disclosed range of "25 to 60%" encompassed the claimed range even though the

claimed range was not expressly taught. The response asserts that simarly the instantly recited "at least 60" and "at least 90" are encompassed by thte specificaiton teaching of "smaller or larger arrays" than those containing 100,000 genomic fragments. This response has been thoroughly reviewed but not found persuasive. The instantly recited "at least 60" and "at least 90" is not similar to that of *In re Wertheim* because the instantly recited limitation of "at least 60" and "at least 90" does not have specified end points that were contemplated in the specification. The specificaiton does not contemplate more than 500,000 probes and "at least 60" and "at least 90" encompass more than 500,000 probes and thus there is no support for an open-end range of "at least 60" and "at least 90". *In re Wertheim* demonstrated that the a range within the disclosed range was supported because the specificaiton provided support for a larger range (25 to 60%) with specific examples of the end point of the claimed ranges (36% and 50%). In the instant case, the claims are not drawn to specified end points which are contemplated within the specification and thus the recitation of "at least 60" and "at least 96" constitute new matter. For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

New Grounds of Rejection, Necessitated by Amendment

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 3, 5-6, 8-9, 11, 13-14, and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ezaki et al. (Int. J. Sys. Bacteriol. 1989, vol. 39, pp. 224-229) in view of Hayward et al. (Mol. Microbiology, 2000, 35(1), 6-14) as evidenced by DiResi (cited on 892 filed 11/19/2003).

Ezaki et al. teach a method of identifying bacteria by providing DNA-DNA hybridization from renaturation rates to determine genetic relatedness and thus identify bacterial species (see pg. 224, 1st column, 1st two para). Ezaki et al. teach DNA of bacterial strains were added to micro dilution plate (microchip, claim 5) (see pg. 224, 1st column, last para con't to 2nd column). Ezaki et al. teach hybridizing of DNA in micro dilution wells (see pg. 224, 2nd column, last para) followed by detection of hybridized DNA (see pg. 225, 1st column). Ezaki et al. teach analysis of at least four reference bacteria strain hybridization (reference strains, table 1). Ezaki et al. teach determining the presence of 70% homology (see figure 4) using fluorescently labeled reference DNA. Ezaki et al. teach identification without sequencing of pathogenic bacteria (see figure 4, 5, 8 and pg. 227, 1st column, last para). Ezaki et al. does not teach providing amplified

random genomic sequences to create a plurality of arrayed elements, nor teach labeled target DNA with a first fluorescent dye and labeled reference DNA from a second fluorescent dye.

Hayward et al. teach constructing a shotgun DNA microarray using random inserts from a genomic library and allows for analysis of genomes that have not been fully sequenced (see abstract). Hayward teach constructing a DNA microarray by printing 3648 PCR inserts from a DNA library amplified (at least 96 arrayed elements, claims 22-25). Hayward et al. teach amplified inserts from 8000 independent clones were applied to the array and the average size was 1-2 kb (see pg. 7, array construction). Hayward teach labeling two different forms of Plasmodium with two different fluorescent labels to evaluate the differences among the two forms (see pg. 7, 2nd column, last paragraph) (labeling with a first and second fluorescent dye). Hayward teach that fluorescence signals from Cy3 and Cy5 label were separately measured at each spot on the array and the red/green fluorescence ratio provided a measure of the relative abundance of the transcripts (see pg. 8, 1st column, 1st para) (calculating a ratio of fluorescent signal for target and reference at each element). It is noted that Hayward teaches hybridized cDNA on glass arrays were processed and analyzed for fluorescence as previously described by DeRisi. DeRisi et al. reference discloses that processing and recording of signals comprises calculation of a hybridization signal intensity ratio and normalization of the signal (claims 6, 14, 26 and 27) (see footnote 49 of DeRisi), accordingly it is an inherent property of the method of Hayward to include such a step.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of determining the identification of a bacteria by DNA-DNA hybridization based upon homology using a micro dilution plate

comprising a plurality of DNA from multiple organisms as taught by Ezaki to include a shotgun DNA microarray from multiple organisms and analysis of hybridization using fluorescently labeled test and reference DNA as taught by Hayward to allow for a more robust analysis of phenotyping organisms without the need for sequencing the genome and an analysis method that allows for a high throughput analysis of bacterial species identification. The ordinary artisan would have been motivated to substitute the micro dilution plate of Ezaki for the shotgun microarray taught by Hayward and thus include the method of constructing as well as the analysis of the shotgun DNA microarray as taught by Hayward in the method of Ezaki because neither Ezaki et al. nor Hayward require the knowledge of known genomic sequences and Hayward teach that the microarray allows for analysis of genomes that have not yet been sequenced and the shotgun microarray and analysis taught by Hayward allows for high throughput analysis with minimal amount of DNA. Furthermore, because both Ezaki and Hayward teach analysis of genomic sequences of pathogenic organisms by DNA hybridization of microarrays, it would have been obvious to one of ordinary skill in the art to substitute one method, the construction of the shotgun microarray as taught by Hayward for the DNA attachment to micro dilution plates as taught by Ezaki in order to achieve the predictable result of detecting bacterial species using DNA hybridization patterns using a shotgun DNA microarray.

11. Claims 2, 4 and 10, 12 rejected under 35 U.S.C. 103(a) as being unpatentable over Ezaki et al. (Int. J. Sys. Bacteriol. 1989, vol. 39, pp. 224-229) in view of Hayward et al. (Mol. Microbiology, 2000, 35(1), 6-14) as evidenced by DiResi (cited on 892 filed 11/19/2003).as applied to claim 1, 3, 5-6, 8-9, 11, 13-14, and 22-27 above, and further in view of Gingeras (US Patent 6228575).

The method of Ezaki in view of Hayward as evidence by DiResi is set forth in section 10 above. Ezaki in view of Hayward as evidence by DiResis does not teach the test sample is from a sample from a subject or environmental isolate.

Gingeras et al. teach a method of oligonucleotide array for speculating and phenotyping organism by providing an array of known locations on a substrate comprising a plurality probes to reference DNA sequences hybridizing target nucleic acid sequence to array and based on hybridization pattern identifying the genotype of the first organisms(see column 3, lines 1-13 and column 4, lines 7-13). Gingeras et al. teach assaying biological samples, which refers to a sample obtained from an organism or clinical sample from a patient (See column 8, lines 22-34) (claims 2 and 10). Gingeras et al. teach assaying biological samples obtained from an organism (environmental sample) (see column 8, lines 22-25) (claims 4 and 12).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of determining the species of an organism by providing a substrate comprising a plurality probes to reference DNA sequences as taught by Ezaki in view of Hayward as evidence by Desiri to include test bacteria that is pathogenic and obtained from samples from a subject as well as environmental isolated, as taught by Gingeras, to improve the method of identification of bacteria species as taught by Ezaki in view of Hayward as evidence by Desiri. The ordinary artisan would have been motivated to improve the method of identifying bacteria to include test bacteria obtained from subjects, environmental isolates, as well as test bacteria that was pathogenic because Gingeras teach a method of bacteria identification that includes pathogenic bacteria obtained from subjects and environmental isolated. Furthermore, because both Ezaki, Hayward, and Gingeras teach analysis of genomic

sequences of pathogenic organisms by DNA hybridization of microarrays, it would have been obvious to one of ordinary skill in the art to substitute the type of test bacteria being analyzed, bacteria from a subject or environmental isolated as taught by Gingeras for the bacteria tested in Ezaki in view of Hayward as evidence by Desiri in order to achieve the predictable result of detecting bacterial species using DNA hybridization patterns using a DNA microarray.

Response to Arguments

12. It is noted that the rejections presented in section 10 and 11 are new grounds of rejection however applicants remarks with regard to Hayward et al. may also pertain to the rejections above. Applicants assert that Hayward teaches away from the claimed invention in that Hayward teaches using reference genomic sequences that contain unknown sequences(see pg 19, section B) and teaches "limitations of the shotgun approach" (see pg. 16, section B). First it is noted that the claims do not require that the sequences of the reference strains sequences are known and the claims *require* a microarray that has amplified random genomic sequences that are unknown, thus the microarray of the claimed invention require that the sequences are unknown, which is taught by Hayward. Additionally, the "limitations of the shotgun approach" taught by Hayward is with regard to the use of the microarray, the section that applicant is pointing to teach away refers to using the microarray for analysis of gene expression, in which case it is advantageous to know the sequence of the gene of interest, however this section is silent with regard to this being a limitation for identification of bacteria species, in fact for identification of unknown bacteria, it is an advantage of the shotgun microarray of Hayward that

the sequence is not known as this allows for analysis of bacteria genomes which haven't yet been sequenced (see abstract and pg. 9, advantages of the shotgun approach).

Conclusion

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571)272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Sarae Bausch, PhD/
Primary Examiner
Art Unit 1634